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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,296	08/06/2002	Maurice Israel	033525-002	9468

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EXAMINER

EMCH, GREGORY S

ART UNIT	PAPER NUMBER
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1649

DATE MAILED: 09/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/049,296

Applicant(s)

ISRAEL ET AL.

Examiner

Gregory S. Emch

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– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 July 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 46-70 is/are pending in the application.
- 4a) Of the above claim(s) 57-70 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 46-56 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 57-70 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Formal Matters***

Claims 17-45 were canceled and new claims 46-70 were added in the communication dated July 5, 2005. Claims 46-70 are pending. Claims 57-70 are withdrawn from consideration as being directed to a non-elected invention. Currently, claims 46-56 are under consideration.

### ***Specification***

The objection to the abstract in the office action dated January 5, 2005 is hereby withdrawn in view of Applicant's amendment.

The objection to the disclosure in the office action dated January 5, 2005 is hereby withdrawn in view of Applicant's amendment.

### ***Response to Amendment and Arguments***

The rejections of claims 17, 18, 20, 21 and 24 under 35 U.S.C. 102 (b) as being anticipated by Helme-Guizon et al. are rendered moot by cancellation of the claims and are thus withdrawn.

The rejections of claims 24, 25, and 26 under 35 U.S.C. 102 (b) as being anticipated by Garthwaite et al. are rendered moot by cancellation of the claims and are thus withdrawn.

The rejections of claims 17 and 26 under 35 U.S.C. 112, second paragraph are rendered moot by cancellation of the claims and are thus withdrawn. . Further, the phrase "mammal Krebs solution" is defined by the specification and the Examiner agrees that one of skill in the art would understand the metes and bounds of said phrase from reading the specification.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Newly presented claims 46-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Reddy & Sastry (25 May 1979; Brain Research 168(2): 287-298), for reasons of record set forth in the Office Action of January 5, 2005 as applied to claims 17-26.

The newly presented claims are directed to a method of preparing calibrated pieces of mammalian cerebral tissue, the method comprising: (i) obtaining one or more samples of mammalian cerebral nerve tissue, (ii) cutting the one or more samples into pieces, (iii) washing the pieces in mammal Krebs solution, (iv) passing the pieces through at least one grid having a mesh size to produce calibrated pieces of mammalian

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cerebral material having a mean size between  $0.1 \text{ mm}^3$  and  $5 \text{ mm}^3$ , and (v) harvesting the calibrated pieces of mammalian cerebral tissue.

In the communication dated July 5, 2005, Applicant argues that the rejection cannot be applied to new claims 46-56 because Reddy & Sastry fail to disclose every element of the claimed invention. Further, Applicant states that the volume of a geometric cube having as its dimension  $433 \mu\text{m}$  on a side (the largest mesh size used by Reddy and Sastry) mesh size is  $(0.433 \text{ mm})^3 = 0.081 \text{ mm}^3$ . Applicant asserts that this is substantially smaller than the pieces of mammalian cerebral tissue prepared according to the method of claim 46 and its dependant claims and that it would be understood that the pieces would not actually be geometric cubes. The pieces of soft tissue would necessarily have rounded edges and corners so that the maximum average volume of the resulting pieces may be better estimated by modeling the pieces as spheres than as cubes. Finally, Applicant asserts that the volume of a sphere having a diameter as large as Reddy and Sastry's largest pore size of  $0.433$  is given by the formula  $\frac{4}{3} \pi r^3 = 0.042 \text{ mm}^3$  which is less than  $1/2$  the smallest  $0.433 \text{ mm}$ , which is less than  $1/2$  the smallest size of the calibrated pieces of mammalian cerebral tissue produced according to the method of claim 46. Furthermore, Applicant argues that Reddy & Sastry only teach the relative amounts of tissue and solution and not to the volume (i.e. size) of the cut pieces and only teach mincing, which does not suggest a calibrated cutting or even any deliberate attempt to produce pieces of tissue of a given size.

Applicant's argument has been fully considered and is not found persuasive.

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Applicant's reasoning and asserted formulas for the calculation of size of the pieces of mammalian cerebral tissues cannot be accepted since the arguments of counsel cannot take the place of evidence in the record. In *re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In *re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Furthermore, the asserted limitation of "calibrated cutting" is not present in the claims as written, and it is inherent for tissue to be "calibrated" after being passed through mesh of a given size. Therefore, in the absence of evidence to the contrary, the nylon bolting cloth taught by Reddy & Sastry teaches mesh sizes that would produce tissue sizes falling into the range of  $0.1 \text{ mm}^3$  and  $5 \text{ mm}^3$  thus meeting the limitations of claim 46 (pp. 289).

Reddy & Sastry teach a method of isolating a preparation of rat cerebral tissue comprising mincing said tissue in Krebs-Ringer solution, then passing said tissue in Krebs-Ringer solution through a nylon bolting cloth, and harvesting the resulting tissue thus meeting the limitations of claims 46, 49, and 50 (pp. 289).

The tissue is minced in a small volume of 1 ml/g tissue that would result in tissue roughly equivalent to the claimed volume of 1 to  $2 \text{ mm}^3$ , thus meeting the limitations of claim 53.

The rat cerebral samples consisted of "whole brain" preparations defined by Reddy & Sastry as "cortex, cerebellum, and brain stem" thus meeting the limitations of claims 47 and 49 (pp. 288-289). Reddy & Sastry also teaches the dissection of the brain preparations into three anatomical regions, the cortex, cerebellum and brain stem thus meeting the limitations of claim 48 (p. 289).

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Reddy & Sastry teaches that the tissue preparation was left in a 25 mL conical tube, due to the force of gravity the cubed tissue would fall to the bottom of the tube being equivalent to "spontaneous sedimentation" thus meeting the limitations of claim 54 (p. 289).

Reddy & Sastry also teach the brain composition (the isolation thereof) as described above, thus meeting the limitations of claims 55 and 56 (pp. 288-289).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Newly presented claims 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reddy & Sastry (25 May 1979; Brain Research 168(2): 287-298).

The claims are directed to a method of preparing calibrated pieces of mammalian cerebral tissue, the method comprising: (i) obtaining one or more samples of mammalian cerebral nerve tissue, (ii) cutting the one or more samples into pieces, (iii) washing the pieces in mammal Krebs solution, (iv) passing the pieces through at least one grid having a mesh size to produce calibrated pieces of mammalian cerebral material having a mean size between  $0.1 \text{ mm}^3$  and  $5 \text{ mm}^3$ , and (v) harvesting the calibrated pieces of mammalian cerebral tissue, wherein said mesh size is between 0.5 mm and 2 mm, or wherein said mesh size is between 1 mm and 2 mm.

Reddy & Sastry teach a method of isolating a preparation of rat cerebral tissue comprising mincing said tissue in Krebs-Ringer solution, then passing said tissue in Krebs-Ringer solution through a nylon bolting cloth, and harvesting the resulting tissue (p. 289). Reddy & Sastry teaches that the nylon bolting cloth used had mesh sizes of  $433 \mu\text{m}$  which corresponds to 0.433 mm mesh size which falls approximately into the range of 0.5 and 2 mm, thus meeting the limitations of claim 51 (p. 289). Reddy & Sastry do not teach mesh sizes of between 0.5 mm and 2 mm or mesh sizes of between 1 mm and 2 mm. However, in the instant case the size of the pieces of neural tissue is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal size of tissue pieces by varying



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the mesh size in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of tissue amount would have been obvious at the time of applicant's invention.

Accordingly, claim 52 is rejected under 35 U.S.C. 103(a).

### ***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

***Advisory Information***

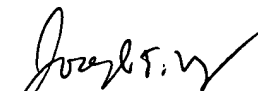
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached on Monday through Friday from 8:30AM to 5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gregory S. Emch, Ph. D.  
Patent Examiner  
Art Unit 1649  
September 13, 2005



**JOSEPH MURPHY**  
**PATENT EXAMINER**